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10/630,446	07/29/2003	Navin Vaya	1296-015	7784

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EXAMINER	
MERCIER, MELISSA S	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
09/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/630,446	VAYA ET AL.	
	Examiner	Art Unit	
	MELISSA S. MERCIER	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7,11-15,18-27,30-33,36-39,43,45-47 and 50-74* is/are pending in the application.

4a) Of the above claim(s) *30,31,73 and 74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-7, 11-15, 18-27, 32-33, 36-39, 43, 45-47, and 50-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

Receipt of Applicants Remarks and Amended Claims filed on June 11, 2009 is acknowledged. Claims 1, 4-7, 11-15, 18-27, 30-33, 36-39, 43, 45-47, and 50-74 remain pending in this application. Claims 30-31 and 73-74 remain withdrawn from consideration as reading on non-elected species.

Maintained Rejections/Objections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-7, 11-15, 18-27, 32-33, 36-39, 43, 45-47, and 50-72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1, 11, 18-19, 33, 43, and 50-51, it is unclear what the units of measure for ratios presented are in. The examiner has interpreted the ratios to be weight ratios.

Regarding claims 5, 7, 13, 37, 39, it is unclear what Applicant is claiming by ammonio methacrylate copolymers type A and B as described in the USP and methacrylic acid copolymer type A, B, and C, as described in the USP. The claims

must be presented to define the invention within the metes and bounds of the specification. The citation to outside sources is outside the specification.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. Applicant argues in the pharmaceutical arts, solid dosage forms are only formulated by weight and not by volume and thus the rations would be always understood to be by weight. The Examiner respectfully disagrees. There is no uniformly accepted definition for "ratio" within the pharmaceutical arts. It is suggested that Applicant amend the claims to recite "weight ratio" since Applicant discloses that support is present in the specification in paragraphs 0016-0017 to remove any indefiniteness in the claim language.

Applicant's arguments regarding the citation of USP are also not persuasive. Applicant contends that citations to an outside source is within the metes and bounds of the specification because although the USP may change its standards, it does not mean that it is improper in a patent claim to refer to that standard because the original standard, if changed, will still be ascertainable. The Examiner respectfully disagrees. Patent claims must stand on their own without reference to outside source. Nor is it the case that there will be historical documents which preserve antiquity.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 4-7, 11-15, 18-27, 32-33, 36-39, 43, 45-47, and 50-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Timmins et al. (US Patent 6,660,300) in view of Boswell (US Patent 3,048,526).

Timmins discloses a controlled release delivery system for pharmaceuticals which have high water solubility, such as antidiabetic metformin HCl salt. The delivery system includes (1) an inner solid particulate phase formed of substantially uniform granules containing a pharmaceutical having a high water solubility, and one or more hydrophilic polymers, one or more hydrophobic polymers and/or one or more hydrophobic materials such as one or more waxes, fatty alcohols and/or fatty acid esters, and (2) an outer solid continuous phase in which the above granules of inner solid particulate phase are embedded and dispersed throughout, the outer solid continuous phase including one or more hydrophobic polymers, one or more hydrophobic polymers and/or one or more hydrophobic materials such as one or more waxes, fatty alcohols and/or fatty acid esters, which may be compressed into tablets (abstract). Timmins discloses high water solubility to be solubility in water at ambient temperature of at least about 50mg/mL water (column 9, lines 40-46).

The inner solid particulate phase may comprise 10-98% drug (column 9, lines 59-61). The extended release material in the form of hydrophobic polymers and/or other hydrophobic materials is in the range of about 5-95% by weight, based on the weight of the inner solid particulate phase (column 9, lines 62-67), which reads on the claimed weight ratio of drug: polymer particles of 100:2.5 to 100:30 as recited in the instant claims.

The inner solid particulate phase is in a weight ratio to the outer solid continuous phase is within the range of 0.5:1 to 4:1 (column 9, lines 54-58), which reads on the claimed weight ratio of particles: coating of 100:2.5 to 100:30 as recited in the instant claims.

The metformin may be used in combination with another anti-hyperglycemic and/or hypolipidemic agent within the same dosage unit in a weight ratio from about 0.01:1 to about 300:1 (column 12, lines 24-32).

Regarding claims 22, 53-55, and 68-69, Suitable additional anti-hyperglycemic drugs include glyburide, glimepiride, glipizide, gliclazide, chlorpropamide, acarbose, miglitol, or thiazolidinediones including rosiglitazone, for example (column 12, line 47-column 13, line 44).

Regarding claims 4-6, 12-13, 36-39, and 45-47, hydrophobic polymers which may be employed in the inner solid particulate phase and/or outer solid continuous phase include, but are not limited to ethyl cellulose, hydroxyethylcellulose, ammonio methacrylate copolymer, methacrylic acid copolymers, methacrylic acid-acrylic acid ethyl ester copolymer, methacrylic acid esters neutral copolymer, dimethylaminoethylmethacrylate-methacrylic acid esters copolymer, vinyl methyl ether/maleic anhydride copolymers, their salts and esters (column 10, lines 44-55).

Regarding claims 14-15, and 46-47, other hydrophobic materials which may be employed in the inner solid particulate phase and/or outer solid continuous phase include, but are not limited to waxes such as beeswax, carnauba wax, microcrystalline wax, and ozokerite; fatty alcohols such as cetostearyl alcohol, stearyl alcohol; cetyl

alcohol and myristyl alcohol; and fatty acid esters such as glyceryl monostearate, glycerol monooleate, acetylated monoglycerides, tristearin, tripalmitin, cetyl esters wax, glyceryl palmitostearate, glyceryl behenate, and hydrogenated castor oil (column 10, lines 56-65).

Regarding claims 23-25, 56-61, highly water soluble drugs, such as metformin, will be employed in a dosage range of 150-3000mg on a regimen in single daily doses or 2-4 divided daily doses, 1-4 times a day (column 20, lines 21-28).

Applicants attention is drawn to the table on the top of column 21 and Examples 1-4, which discloses 28-39% released at 1 hour, and between 75.7 through 93.1 at 6hrs (columns 21-23: Examples 1-4). Since the prior art discloses the same composition as the instant claims, it is the position of the examiner that it would possess the same functional properties at the instant claims, with regard to plasma concentrations.

Timmins does not disclose the top surface of the tablet not being covered by the outer portion.

Boswell disclosed medicinal tablet preparation containing substantially segregated quantities of the same or different ingredients (column 1, lines 7-10). Inlay tablets are disclosed (column 2, line 62-column 3, line 68).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Timmins with the tablet of Boswell in order to provide sustained-release of an active pharmaceutical with immediate release of another or the same active pharmaceutical.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have optimized the ratio of particles to coating in order to alter the drug release profile. Timmins discloses, in a controlled release dosage form, the formulator tries to reduce the rate of dissolution by, for example, embedding the drug in a polymeric matrix or surrounding it with a polymeric barrier membrane through which drug must diffuse to be released for absorption. To reduce the rate of release of drug from the dosage form to an appropriate level consistent with the blood level profile desired for a drug possessing very high water solubility, very large amounts of polymer would be required for the matrix or barrier membrane. If the total daily dose of drug to be delivered is of the order of only a few milligrams this may be feasible, but many drugs having the solubility properties described require total daily doses of the order of many hundreds of milligrams. Whilst it is possible to create oral controlled release dosage forms for such products by use of large amounts of polymer, an unacceptably large dosage form may result (column 2, lines 16-33).

Applicant is reminded that where the general conditions of the claims are met, burden is shifted to applicant to provide a patentable distinction. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. See In re Aller, 220 F.2d 454 105 USPQ 233,235 (CCPA 1955). The optimization of the polymer coating would be a rate limiting/controlling variable.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. Applicant argues:

***Timmins requires the use of a hydrophilic polymer.**

While the reference may require additional components, it is noted that Applicant has employed comprising language allowing for such an inclusion.

***Timmins final dosage form would be unappealing due to its size.**

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., final size of the dosage unit) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

***Timmins discloses a much higher percentage of polymer that in the instant claims.**

Timmins discloses the inner solid particulate phase may comprise 10-98% drug (column 9, lines 59-61). The extended release material in the form of hydrophobic polymers and/or other hydrophobic materials is in the range of about 5-95% by weight, based on the weight of the inner solid particulate phase (column 9, lines 62-67), which reads on the claimed weight ratio of drug: polymer particles of 100:2.5 to 100:30 as recited in the instant claims.

The inner solid particulate phase is in a weight ratio to the outer solid continuous phase is within the range of 0.5:1 to 4:1 (column 9, lines 54-58), which reads on the claimed weight ratio of particles: coating of 100:2.5 to 100:30 as recited in the instant claims.

The recited claims within Timmins overlap the ratios of the instant claims.

***Timmins does not disclose any enabled examples comprising additional antihyperglycemic compounds.**

Applicant is reminded that a patent is presumed enabled for all that it discloses. While there may be no direct example of a composition comprising two different antihyperglycemic compounds, Timmins discloses that they can be used. Applicant has not provided any evidence that the teachings of Timmins are not enabled for such a combination.

***The teachings of Boswell do not disclose a compact sustained release dosage form of high dose, highly soluble drugs in combination with low dose active.**

It is respectfully submitted that Boswell is not relied on for the teachings of the high dose, highly soluble drugs in combination with low dose active but rather that the inlay dosage form is known in the art.

***Applicant has additionally presented photos of the instantly claimed tablet and the tablet of Timmins.**

It is unclear to the Examiner what argument Applicant is attempting to make with the tablet pictures. Clarification is requested. Applicant has previously argued that the

Timmins final product size is larger than the instantly claimed tablet; however, as discussed above, such a limitation is not in the claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA S. MERCIER whose telephone number is (571)272-9039. The examiner can normally be reached on 8:00am-4:30pm Mon through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Melissa S Mercier/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615